Access DB# 39027

SEARCH REQUEST FORM

Scientific and Technical Information Center

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Requester's Full Name: San Hui Examiner #: 78222 Date: 3/30/01
Art Unit: 1617 Phone Number 305-1002 Serial Number: 09/666146
Mail Box and Bldg/Room Location: _____ Results Format Preferred (circle): PAPER DISK E-MAIL
↳ 2B19 ↳ CM1/2A12

If more than one search is submitted, please prioritize searches in order of need.

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Please provide a detailed statement of the search topic, and describe as specifically as possible the subject matter to be searched. Include the elected species or structures, keywords, synonyms, acronyms, and registry numbers, and combine with the concept or utility of the invention. Define any terms that may have a special meaning. Give examples or relevant citations, authors, etc, if known. Please attach a copy of the cover sheet, pertinent claims, and abstract.

Title of Invention: Method for the therapeutic management of extrauterine proliferation of endometrial tissue, chronic pelvic pain

Inventors (please provide full names): Hilde Rechmueller-Winzen, Ingwer Engel, Ricardo Felberbaum, Klaus Diedrich, Wolfgang Kunker

Earliest Priority Filing Date: 9/23/1999

***For Sequence Searches Only* Please include all pertinent information (parent, child, divisional, or issued patent numbers) along with the appropriate serial number.**

I would like to ask Susan Hanley to perform the search

Please search claims 1-13. The method claims for treating extrauterine proliferation of endometrial tissue Mynic pelvic pain and/or fallopian tube obstruction (FTO). ing the compounds herein.

Thanks.

Point of Contact:
Susan Hanley
Technical Info. Specialist
CM1 12C14 Tel: 305-4053

L1

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STAFF USE ONLY

Searcher: Hanley
Searcher Phone #: _____
Searcher Location: _____
Date Searcher Picked Up: 4/4
Date Completed: 4/17
Searcher Prep & Review Time: _____
Clerical Prep Time: _____
Online Time: _____

Type of Search

NA Sequence (#) _____
AA Sequence (#) _____
Structure (#) _____
Bibliographic _____
Litigation _____
Fulltext _____
Patent Family _____
Other _____

Vendors and cost where applicable

STN 3a7
Dialog _____
Questel/Orbit _____
Dr.Link _____
Lexis/Nexis _____
Sequence Systems _____
WWW/Internet _____
Other (specify) _____

PTO-1590 (1-2000)

=> d bib abs hitrn 1

L38 ANSWER 1 OF 2 HCAPLUS COPYRIGHT 2001 ACS
AN 1996:128826 HCAPLUS
DN 124:250979
TI Established hormonal chemoprevention of endometrial and ovarian cancer, and prospects for hormonal chemoprevention of breast cancer
AU Pike, M. C.; Spicer, D. V.
CS School Medicine, University Southern California, Los Angeles, CA, USA
SO Contrib. Oncol. (1995), 50(Hormone-Dependent Tumors), 299-323
CODEN: COONEV; ISSN: 0250-3220
DT Journal; General Review
LA English
AB A review, with 70 refs., on the development of a combination-type oral contraceptive based on a LH-RH agonist with add-back very low dose sex steroids that would protect women against endometrial, ovarian and breast cancers.
IT 9034-40-6, LHRH
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(agonists; LH-RH agonist based oral contraceptive for prevention of breast and endometrial and ovarian cancers in women)

=> d bib abs hitrn 2

L38 ANSWER 2 OF 2 HCAPLUS COPYRIGHT 2001 ACS
AN 1990:491542 HCAPLUS
DN 113:91542
TI Intermittent GnRH antagonist plus progestin contraception conserving tonic ovarian estrogen secretion and reducing progestin exposure
AU Danforth, Douglas R.; Williams, Robert F.; Hsiu, Jeng G.; Roh, Sung I.; Hahn, DoWon; McGuire, John L.; Hodgen, Gary D.
CS Jones Inst. Reprod. Med., East. Virginia Med. Sch., Norfolk, VA, 23510, USA
SO Contraception (1990), 41(6), 623-31
CODEN: CCPTAY; ISSN: 0010-7824
DT Journal
LA English
AB The effectiveness of a once-weekly regimen of LH-RH antagonist followed by a progestin as a potential new contraceptive method was studied in monkeys. On menstrual cycle days 2, 9, 16, and 23 (onset of menses = day 1) monkeys were divided into 2 groups: those injected s.c. with 0.1 mg/kg Nal-Glu LH-RH antagonist in saline and those given only vehicle (control). On cycle days 15-26, each treated female was administered 25 .mu.g norgestimate/day orally. This was continued for 3 treatment cycles (84 days). Weekly injections of Nal-Glu LH-RH antagonist effectively blocked completion of folliculogenesis, ovulation, and corpus luteum function as judged by serum LH, estradiol, and progesterone. Serum progesterone was undetectable (<0.1 ng/mL) during the treatment cycles. Importantly, serum estradiol levels during LH-RH antagonist plus norgestimate treatments were maintained at 35 pg/mL. Upon the cessation of norgestimate treatment on day 26 in each cycle, menses uniformly began within 2 or 3 days. Regarding recovery, apparently normal and presumably ovulatory menstrual cycles, as judged by timely estradiol elevations, midcycle LH surges, and luteal phase progesterone patterns, were manifest immediately following termination of the final LH-RH antagonist plus norgestimate treatment cycle. Endometrial biopsies removed on day 26 of control cycles and on day 26 of the third treatment cycle revealed appropriate late secretory phase endometrium having tortuous endometrial glands and superficial stromal edema. Histol. sections of ovaries removed at the end of the LH-RH antagonist plus norgestimate treatment revealed multiple small and medium-sized developing and atretic follicles, having maintained serial ablation of the potentially maturing follicles. Apparently, once-weekly LH-RH antagonist plus norgestimate treatment is a feasible method of ovulation inhibition. The intermittent (weekly) LH-RH antagonist regimen allows follicular estradiol prodn. to continue at tonic levels. Transformation of secretory to proliferative endometrium by the 12 day/mo progestin regimen attenuated the potentially adverse effects of unopposed estrogen on target tissues.
IT 9034-40-6, LH-RH
RL: BIOL (Biological study)
(antagonists, contraceptive activity of progestin and intermittent administration of)

=> d bib abs hitrn 1

L39 ANSWER 1 OF 7 HCAPLUS COPYRIGHT 2001 ACS
AN 1997:364766 HCAPLUS
DN 127:45030
TI A hormonal contraceptive approach to reducing breast and ovarian cancer risk: an update
AU Pike, M. C.; Daniels, J. R.; Spicer, D. V.
CS Departments of Preventive Medicine and Medicine, USC/Norris Comprehensive Cancer Center, Los Angeles, CA, 90033-0800, USA
SO Endocr.-Relat. Cancer (1997), 4(1), 125-133
CODEN: ERCAE9; ISSN: 1351-0088
PB Journal of Endocrinology
DT Journal; General Review
LA English
AB A review with 20 refs. Epidemiol. studies have consistently found that bilateral oophorectomy at a young age substantially reduces breast cancer risk. Such surgical menopause around age 35 has been found to reduce risk by 60 to 75%. A reversible medical oophorectomy using an agent such as a gonadotropin-releasing hormone agonist (GnRHa) should achieve a similar redn. in risk. Although the use of GnRHa alone is unacceptable because of the assocd. hypoestrogenic side-effects, these can be satisfactorily prevented by add-back low-dose estrogen treatment with intermittent progestin to protect the endometrium. It is estd. that a regimen of GnRHa plus add-back ultra low-dose estrogen and progestin would prevent some two-thirds of current breast cancer if used from age 30. If used from age 20 almost nine out of ten current breast cancer cases would be avoided. If, as is likely, these ests. also apply to women at high genetic risk of breast cancer because of possession of a BRCA1 or BRCA2 gene, their breast cancer risk would be reduced to below that of "normal" women. The protective effects on ovarian cancer are calcd. to be greater than the protective effects on breast cancer. Practical chemoprevention of breast and ovarian cancer using this approach should be possible within 5 yr.
IT 9034-40-6, LH-RH
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(a hormonal contraceptive approach to reducing breast and ovarian cancer risk)

=> d bib abs hitrn 2

L39 ANSWER 2 OF 7 HCAPLUS COPYRIGHT 2001 ACS
AN 1997:168540 HCAPLUS
DN 126:152828
TI LHRH antagonist synthetic peptide analogs for use as cancer inhibitors, contraceptives, or other pharmaceuticals
IN Roeske, Roger W.
PA Indiana University Foundation, USA; Roeske, Roger W.
SO PCT Int. Appl., 52 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9640757	A2	19961219	WO 1996-US9852	19960607
	WO 9640757	A3	19970220		
	W: AU, CA, JP, US				
	RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
	US 5843901	A	19981201	US 1995-480494	19950607
	CA 2219460	AA	19961219	CA 1996-2219460	19960607
	AU 9661680	A1	19961230	AU 1996-61680	19960607
	AU 715399	B2	20000203		
	EP 794961	A2	19970917	EP 1996-919311	19960607
	R: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
	JP 11507374	T2	19990629	JP 1996-502050	19960607
PRAI	US 1995-480494		19950607		
	WO 1996-US9852		19960607		

OS MARPAT 126:152828
AB Many novel LH-releasing hormone(LHRH) antagonist peptide analogs or peptide mimetics, pharmaceutical compns. thereof, and methods of use thereof, are disclosed. The LHRH antagonist comprises a peptide compd., wherein a residue of the peptide compd. corresponding to the amino acid at position 6 of natural mammalian LHRH comprises a hydrophilic N-acyl moiety, a dipolar moiety, a sulfonium moiety, a receptor-modifying moiety or a small polar moiety. LHRH antagonist peptides are useful as inhibitors of sex hormone-dependent cancers (e.g., prostate cancer). LHRH antagonist peptides are also useful as contraceptive agents. The peptides can be used to treat other LHRH-related disorders as well, such as precocious puberty or premenstrual syndrome. The anti-ovulatory and histamine release activity of LHRH antagonists are compared. S.c. injections of LHRH antagonists suppressed plasma testosterone levels.
IT 9034-40-6DP, LHRH, analogs
RL: BAC (Biological activity or effector, except adverse); PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(LHRH antagonist synthetic peptide analogs with pharmaceutical applications as cancer inhibitors or contraceptive agents)

=> d bib abs hitrn 3

L39 ANSWER 3 OF 7 HCAPLUS COPYRIGHT 2001 ACS
AN 1991:442156 HCAPLUS
DN 115:42156
TI Intranasal LHRH agonist combined periodically with a progestogen for contraception
AU Lemay, A.
CS Cent. Rech., Hop. St.-Francois d'Assise, Quebec, PQ, Can.
SO Adv. Contracept. (1989), 5(4), 253-62
CODEN: ADCOEB; ISSN: 0267-4874
DT Journal
LA English
AB A discussion is given of data on intranasal formulation studies using an LHRH agonist administered continuously vs. intermittently in sequential combination with a progestogen. In addn., preliminary data are also discussed on the continuous use of a low-dosage intranasal LHRH agonist with periodic addn. of a progestogen in women requiring long-term treatment for recurrent endometriosis or dysfunctional uterine bleeding.
IT 9034-40-6, LHRH
RL: BIOL (Biological study)
(agonist, contraceptive activity of and gynochol. disease treatment with progestogen and, in women)

=> d bib abs hitrn 4

L39 ANSWER 4 OF 7 HCAPLUS COPYRIGHT 2001 ACS
AN 1987:96973 HCAPLUS
DN 106:96973
TI Contraception in dogs with luteinizing hormone releasing hormone antagonists
IN Vickery, Brian H.
PA Syntex (U.S.A.), Inc., USA
SO Eur. Pat. Appl., 19 pp.
CODEN: EPXXDW
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	EP 199302	A2	19861029	EP 1986-105372	19860418
	R: AT, BE, CH, DE, FR, GB, IT, LI, LU, NL, SE				
	AU 8656388	A1	19861023	AU 1986-56388	19860418
PRAI	US 1985-725267		19850419		

AB Contraception in female dogs comprises administering an LH-RH antagonist either during estrus or during pregnancy for a time sufficient to terminate either estrus or pregnancy. Thus, a bitch was bled and plasma progesterone (I) measured in nanograms/mL vs. the day of diestrus. On day -8 and -4 the plasma I was 4-6 ng/mL, at day 1 it was 30 ng/mL, it peaked at 60 ng/mL on day 9, and slowly decreased to 30 ng/mL on day 25. At day 25 the animal was given a daily s.c. injection of [N-Ac-D-Nal(2),1 D-p-Cl-Phe2, D-Trp3, D-Deh6, D-Ala10]LH-RH [D-Nal(2) = 3-(2-naphthyl)-D-alanyl; D-p-Cl-Ph = 3-(p-chlorophenyl)-D-alanyl; D-Deh = NG,NG-diethyl-D-homoarginine] for 7 days. After the 1st injection the plasma I dropped to 4 ng/mL, at the of the treatment the plasma I level was <1 ng/mL, and a fetus was expelled the 5th day of treatment with tissue mass expelled on day 49 which was 24 days after the start of treatment. A s.c. injectable soln. was formulated contg. LH-RH antagonist 10.0, benzyl alc. 9.0, AcOH 1.2, propylene glycol 200.0 and mannitol 35.0 mg, sterile H2O 1.0 mL.

IT 9034-40-6, LH-RH
RL: BIOL (Biological study)
(antagonists, as contraceptive in dog)

=> d bib abs hitrn 5

L39 ANSWER 5 OF 7 HCAPLUS COPYRIGHT 2001 ACS
AN 1986:546417 HCAPLUS
DN 105:146417
TI Morphological studies of human **endometrium** during continuous LH-RH agonist treatment
AU Lundkvist, Oerjan; Bergquist, Christer
CS Dep. Obstet. Gynecol., Univ. Hosp., Uppsala, S-75185, Swed.
SO Int. J. Fertil. (1986), 30(4), 65-70
CODEN: INJFA3; ISSN: 0020-725X
DT Journal
LA English
AB Light and electron microscopic studies were performed on **endometrial** biopsies from healthy women after 2-17 mo of daily intranasal treatment with the LH-RH agonist D-Ser(TBU)6-EA10-LRH [104428-01-5] for contraceptive purposes. Hormone analyses revealed inhibition of ovulation in all the women. Light microscopy showed an inactive or weak proliferative **endometrial** pattern, with no signs of hyperplasia. Ultrastructurally, the epithelial and stromal cells of the **endometrium** displayed signs of low metabolic activity. Since the results are contradictory to those earlier presented by others, further studies are necessary to exclude the potential risk of hyperestrogenic stimulation of the **endometrium** during continuous LH-RH agonist treatment.
IT 9034-40-6D, analog
RL: BIOL (Biological study)
(uterus **endometrium** morphol. response to, as contraceptive in women)

=> d bib abs hitrn 6

L39 ANSWER 6 OF 7 HCAPLUS COPYRIGHT 2001 ACS
AN 1985:464894 HCAPLUS
DN 103:64894
TI Comparison of LH-RH agonist and antagonist: antifertility and therapeutic developments
AU Corbin, Alan; Bex, Frederick J.; Jones, Robert C.
CS Endocr. Sect., Wyeth Lab., Inc., Philadelphia, PA, 19101, USA
SO Int. Congr. Ser. - Excerpta Med. (1984), 656(LHRH Its Analogues), 95-122
CODEN: EXMDA4; ISSN: 0531-5131
DT Journal; General Review
LA English
AB A review, with 25 refs., on the contraceptive and therapeutic activity and potency, under a variety of exptl. conditions, of highly potent LH-RH [9034-40-6] agonists and antagonists. LH-RH analog effects on ovulation, estrous cycle, male reprodn., endometriosis, prostatic carcinoma, and puberty are discussed.

=> d bib abs hitrn 7

L39 ANSWER 7 OF 7 HCAPLUS COPYRIGHT 2001 ACS
AN 1981:598081 HCAPLUS
DN 95:198081
TI Endometrial patterns in women on chronic luteinizing hormone-releasing hormone agonist treatment for contraception
AU Bergquist, Christer; Nillius, Sven Johan; Wide, Leif; Lindgren, Anders
CS Dep. Obstet. Gynecol., Univ. Hosp., Uppsala, S-75014/14, Swed.
SO Fertil. Steril. (1981), 36(3), 339-42
CODEN: FESTAS; ISSN: 0015-0282
DT Journal
LA English
AB Endometrial biopsy specimens were obtained from 12 healthy women under chronic intranasal LH-RH [9034-40-6] agonist treatment for evaluation of the risk of endometrial hyperplasia during long-term inhibition of ovulation. A single daily dose of 400 or 600 .mu.g of the superactive LH-RH agonist Hoe 766 [57982-77-1] was given for 13-55 wk. Treatment was monitored by clin. examn., basal body temp. recordings, and frequently taken venous blood specimens for detn. of estradiol [50-28-2] and progesterone [57-83-0]. Ovulation was inhibited during all but 2 of the 102 treatment cycles. No pregnancy occurred. Six of the women had slight menstrual-like bleeding, and 6 had amenorrhea during the treatment period. No dysfunctional uterine bleeding occurred. The dominating histol. picture of the 17 endometrial biopsies, obtained after 78-380 days of treatment, was inactive or weak proliferative glands with slightly atrophic stroma. There were no signs of hyperplasia. After discontinuation of treatment ovulatory menstrual cycles rapidly returned.
IT 9034-40-6D, analogs
RL: BIOL (Biological study)
(intranasal contraceptive, uterus morphol. response to)

=> d bib abs hitstr 1

L49 ANSWER 1 OF 3 HCAPLUS COPYRIGHT 2001 ACS
AN 2001:73538 HCAPLUS
DN 134:136699
TI Pharmaceutical formulations comprising water-insoluble complex of a peptides for sustained drug delivery
IN Gefter, Malcolm L.; Barker, Nicholas; Musso, Gary; Molineaux, Christopher J.
PA Praecis Pharmaceuticals, Inc., USA
SO U.S., 19 pp., Cont.-in-part of U.S. 5,968,895.
CODEN: USXXAM
DT Patent
LA English
FAN.CNT 2

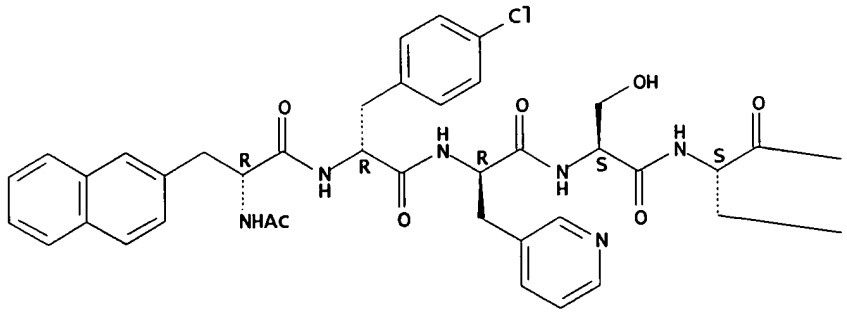
	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 6180608	B1	20010130	US 1997-988851	19971211
	CN 1245436	A	20000223	CN 1997-181608	19961211
	ZA 9710994	A	19980710	ZA 1997-10994	19971208

PRAI US 1996-762747 19961211
OS MARPAT 134:136699
AB Sustained delivery formulations comprising a water-insol. complex of a peptidic compd. (e.g., a peptide, polypeptide, protein, peptidomimetic or the like) and a carrier macromol. are disclosed. The formulations of the invention allow for loading of high concns. of peptidic compd. in a small vol. and for delivery of a pharmaceutically active peptidic compd. for prolonged periods, e.g., one month, after administration of the complex. The complexes of the invention can be milled or crushed to a fine powder. In powd. form, the complexes form stable aq. suspensions and dispersions, suitable for injection. In a preferred embodiment, the peptidic compd. of the complex is an LHRH analog, preferably an LHRH antagonist, and the carrier macromol. is an anionic polymer, preferably CM-cellulose. Methods of making the complexes of the invention, and methods of using LHRH-analog-contg. complexes to treat conditions treatable with an LHRH analog, are also disclosed. Thus, 50 mg of PPI-149 was dissolved in 2 mL of 5% mannitol and mixed with 2 mL of 0.5% CM-cellulose. The mixt. was stirred and immediately yielded a white ppt. The suspension was frozen and lyophilized to dryness to yield a PPI-149 sustained delivery complex.
IT 9034-40-6D, LHRH, analogs 120287-85-6, Cetrorelix
183552-38-7, PPI-149
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(pharmaceutical formulations comprising water-insol. complex of peptides for sustained drug delivery)
RN 9034-40-6 HCAPLUS
CN Luteinizing hormone-releasing factor (9CI) (CA INDEX NAME)

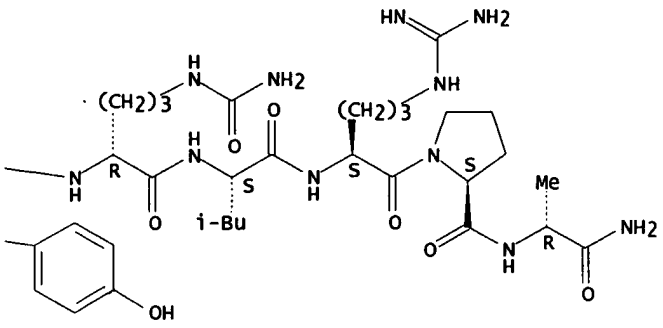
*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
RN 120287-85-6 HCAPLUS
CN D-Alaninamide, N-acetyl-3-(2-naphthalenyl)-D-alanyl-4-chloro-D-phenylalanyl-3-(3-pyridinyl)-D-alanyl-L-seryl-L-tyrosyl-N5-(aminocarbonyl)-D-ornithyl-L-leucyl-L-arginyl-L-prolyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



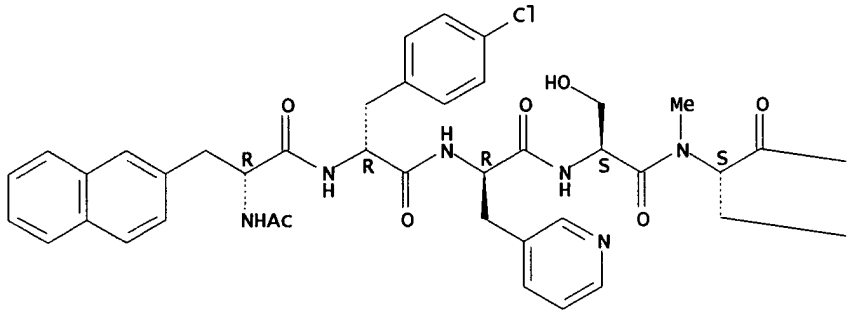
PAGE 1-B



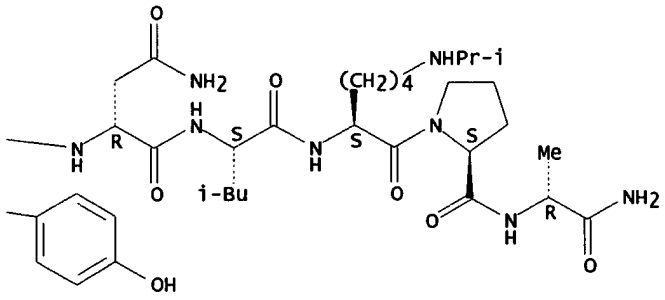
RN 183552-38-7 HCAPLUS
CN D-Alaninamide, N-acetyl-3-(2-naphthalenyl)-D-alanyl-4-chloro-D-phenylalanyl-3-(3-pyridinyl)-D-alanyl-L-seryl-N-methyl-L-tyrosyl-D-asparaginyl-L-leucyl-N6-(1-methylethyl)-L-lysyl-L-prolyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



RE.CNT 42
RE
(1) Anon; FR 2455459 1981 HCAPLUS
(2) Anon; JP 63-310827 1988 HCAPLUS
(3) Anon; WO 8805661 1988 HCAPLUS
(4) Anon; EP 328090 1989 HCAPLUS
(6) Anon; WO 9211844 1992 HCAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> d bib abs hitrn 2

L49 ANSWER 2 OF 3 HCAPLUS COPYRIGHT 2001 ACS
AN 2000:84613 HCAPLUS
DN 132:141952
TI Bioimplant formulations containing stearin
IN Trigg, Timothy Elliot; Walsh, John Desmond; Rathjen, Deborah Ann
PA Peptech Limited, Australia
SO PCT Int. Appl., 37 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2000004897	A1	20000203	WO 1999-AU585	19990720
	W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	AU 9948890	A1	20000214	AU 1999-48890	19990720
PRAI	AU 1998-4730	19980720			
	AU 1998-4731	19980720			
	AU 1999-324	19990513			
	WO 1999-AU585	19990720			

AB A pharmaceutical and/or veterinary formulation comprising about 2-30 % (wt./wt.) of at least 1 active agent, about 0.5-20.0% of a pore-forming agent and the balance stearin. Such formulations provide sustained release of the at least one active agent in humans and other animals for periods of 7 days up to about 2 yr. Stearin and lecithin were mixed with freeze-dried deslorelin. The mixed material was extruded by using a ram extruder and was equilibrated at 55.degree.. The product was then extruded at a rate of 3 g over a 30-s period and cooled and the the long rods produced were sectioned into lengths of the required wt. In dissoln. tests, after an initial rapid release of deslorelin, a sustained release extending over a prolonged period (110 days) was achieved. The av. daily rate of deslorelin release during the sustained release period was within the range 50-2 .mu.g/day.

IT 9034-40-6, GnRH 9034-40-6D, LHRH, analogs
120287-85-6, Cetrorelix 144743-92-0, Teverelix
183552-38-7, Abarelix
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(bioimplant formulations contg. stearin)

RE.CNT 4
RE
(1) Hoffman-La Roche, F; WO 9408623 1994 HCAPLUS
(2) Novo Nordisk AS; US 5179079 1993 HCAPLUS
(3) Peptide Technology Limited; WO 9700693 1997 HCAPLUS
(4) Yamanouchi Pharmaceutical Co; US 4578391 1986 HCAPLUS

=> d bib abs hitrn 3

L49 ANSWER 3 OF 3 HCAPLUS COPYRIGHT 2001 ACS
AN 1998:402333 HCAPLUS
DN 129:86019
TI Pharmaceutical formulations for sustained drug delivery of peptides
IN Gefter, Malcolm L.; Barker, Nicholas; Musso, Gary; Molineaux, Christopher J.
PA Praecis Pharmaceuticals Inc., USA; Gefter, Malcolm L.; Barker, Nicholas; Musso, Gary; Molineaux, Christopher J.
SO PCT Int. Appl., 44 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9825642	A2	19980618	WO 1997-US22881	19971211
	W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
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	CN 1245436	A	20000223	CN 1997-181608	19961211
	ZA 9710994	A	19980710	ZA 1997-10994	19971208
	AU 9856991	A1	19980703	AU 1998-56991	19971211
	EP 952843	A2	19991103	EP 1997-953188	19971211
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
	BR 9714015	A	20000509	BR 1997-14015	19971211
	JP 2000508345	T2	20000704	JP 1998-527002	19971211
PRAI	US 1996-762747	19961211			
	WO 1997-US22881	19971211			

OS MARPAT 129:86019
AB Sustained delivery formulations comprising a water-insol. complex of a peptidic compd. (e.g., a peptide, polypeptide, protein, peptidomimetic or the like) and a carrier macromol. are disclosed. The formulations of the invention allow for loading of high concns. of peptidic compd. in a small vol. and for delivery of a pharmaceutically active peptidic compd. for prolonged periods, e.g., one month, after administration of the complex. The complexes of the invention can be milled or crushed to a fine powder. In powd. form, the complexes form stable aq. suspensions and dispersions, suitable for injection. In a preferred embodiment, the peptidic compd. of the complex is an LHRH analog, preferably an LHRH antagonist, and the carrier macromol. is an anionic polymer, preferably CM-cellulose. Methods of making the complexes of the invention, and methods of using LHRH-analog-contg. complexes to treat conditions treatable with an LHRH analog, are also disclosed. An equal amt. of a 6.25 mg/mL PPI-149 (LHRH antagonist) was added to a soln. of 0.125% CM-cellulose and stirred overnight then filtered. The recovered white paste was rinsed with water and dried for 72 h to obtain 633 mg of a white powder contg. 57% PPI-149.
IT 9034-40-6D, LHRH, analogs 120287-85-6, Cetrorelix 183552-38-7, PPI 149
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(pharmaceutical formulations for sustained drug delivery of peptides)

=> d ind 3

L49 ANSWER 3 OF 3 HCAPLUS COPYRIGHT 2001 ACS
IC ICM A61K038-00
ICS A61K047-48; A61K038-09
CC 63-6 (Pharmaceuticals)
ST pharmaceutical sustained drug delivery peptide; CM cellulose PPI149 sustained drug delivery
IT Electron beams
(irradn.; pharmaceutical formulations for sustained drug delivery of peptides)
IT Antitumor agents
Benign prostatic hyperplasia
Contraceptives

Endometriosis
Fertilization (animal)
Gamma ray irradiation
Intramuscular injections
Oral drug delivery systems
Parenteral solutions (drug delivery systems)
Prostatic tumor inhibitors
Subcutaneous injections
Uterine leiomyoma
(pharmaceutical formulations for sustained drug delivery of peptides)

IT Acrylic polymers, biological studies
Peptides, biological studies
Polymers, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(pharmaceutical formulations for sustained drug delivery of peptides)

IT Puberty
(precocious puberty; pharmaceutical formulations for sustained drug delivery of peptides)

IT 9000-07-1D, Carrageenan, anionic derivs. 9004-32-4 9005-32-7, Alginic acid 9005-38-3, Algin 9034-40-6D, LHRH, analogs 9046-38-2, Polygalacturonic acid 9063-38-1, Sodium starch glycolate 11138-66-2, Xanthan gum 120287-85-6, Cetrorelix 183552-38-7, PPI 149 209122-72-5 209122-73-6
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(pharmaceutical formulations for sustained drug delivery of peptides)

=> d bib abs hitrn 1

L57 ANSWER 1 OF 6 HCAPLUS COPYRIGHT 2001 ACS
AN 2000:15210 HCAPLUS
DN 132:64179
TI Preparation of thienopyridines possessing excellent gonadotropin-releasing hormone antagonizing activity
IN Furuya, Shuichi; Choh, Nobuo; Suzuki, Nobuhiro; Imada, Takashi
PA Takeda Chemical Industries, Ltd., Japan
SO PCT Int. Appl., 111 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2000000493	A1	20000106	WO 1999-JP3379	19990624
	W: AE, AL, AM, AU, AZ, BA, BB, BG, BR, BY, CA, CN, CU, CZ, EE, GD, GE, HR, HU, ID, IL, IN, IS, JP, KG, KR, KZ, LC, LK, LR, LT, LV, MD, MG, MK, MN, MX, NO, NZ, PL, RO, RU, SG, SI, SK, SL, TJ, TM, TR, TT, UA, US, UZ, VN, YU, ZA, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	AU 9943931	A1	20000117	AU 1999-43931	19990624
	EP 1090010	A1	20010411	EP 1999-926797	19990624
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
	JP 3028486	B1	20000404	JP 1999-179206	19990625
	JP 2000219690	A2	20000808		
	JP 2000219691	A2	20000808	JP 1999-273754	19990625
	NO 2000006479	A	20001219	NO 2000-6479	20001219
PRAI	JP 1998-181263	19980626			
	JP 1998-333004	19981124			
	WO 1999-JP3379	19990624			
	JP 1999-179206	19990625			

OS MARPAT 132:64179
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The title compds. [I; R1 = (un)substituted alkyl, cycloalkyl, alkoxyamino, hydroxyamino; R2 = (un)substituted alkyl, Ph (when R1 = unsubstituted alkyl, then R2 = substituted alkyl or substituted Ph)], which possess excellent gonadotropin-releasing hormone antagonizing activity, and are useful for preventing or treating sex hormone-dependent diseases, e.g., sex hormone-dependent cancers (e.g., prostatic cancer, uterine cancer, breast cancer, pituitary tumor), prostatic hypertrophy, hysteromyoma, endometriosis, precocious puberty, amenorrhea syndrome, multilocular ovary syndrome, pimples etc., or as a pregnancy regulator (e.g., contraceptive), infertility remedy or menstruation regulator, were prepd. and formulated. Thus, reacting amine II (prepn. given) with cyclopropanecarboxylic acid in the presence of EtN(iso-Pr)2 and PyBop in CH2Cl2 followed by treatment of free base with HCl soln. in Et2O afforded I.HCl [R1 = cyclopropyl; R2 = iso-Pr] which showed IC50 of 0.06 .mu.M and 0.0001 .mu.M against 125I-leuprorelin binding at rat and human membrane fractions, resp.
RE.CNT 2
RE
(1) Hayase, Y; WO 9741126 A 1997 HCAPLUS
(2) Takeda Chemical Industries Ltd; EP 0781774 A 1997 HCAPLUS

=> d bib abs hitrn 2

L57 ANSWER 2 OF 6 HCAPLUS COPYRIGHT 2001 ACS
AN 1998:502537 HCAPLUS
DN 129:136498
TI Preparation of luteinizing hormone releasing hormone analogs
IN Shaobo, Xiao
PA Asta Medica Aktiengesellschaft, Germany
SO U.S., 15 pp. Cont.-in-part of U.S. Ser. No. 265,631, abandoned.
CODEN: USXXAM
DT Patent
LA English
FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 5783562	A	19980721	US 1995-450951	19950523
	CN 1061605	A	19920603	CN 1990-108955	19901110
	CN 1036343	B	19971105		
PRAI	CN 1990-108955	19901110			
	US 1991-789730	19911112			
	US 1994-265631	19940624			

OS MARPAT 129:136498
AB A method is provided for the design and synthesis of LH -releasing hormone (LHRH) antagonists, e.g. Ac-D-2Nal-D-pClPhe-AA3-Ser-AA5-D-3Pal-Leu-AA8-Pro-D-Ala-NH2 [I; 2Nal = 3-(2-naphthyl)alanine; pClPhe = 4-chlorophenylalanine; AA3 = D-Phe, 3-(3-pyridyl)alanine (D-3Pal); AA5 = Arg, 4-(4-morpholinylmethyl)-L-phenylalanine (Mop); AA8 = Arg, 4-(dipropylaminomethyl)-L-phenylalanine], having exact amino acid sequences and contg. 5-100 amino acids. This method can be used to produce peptides useful in treating disorders of the reproductive endocrine system, including endometriosis, precocious puberty, prostate cancer and breast cancer. Addnl., peptides produced by this method can be used as contraceptives for either males or females. Peptides produced by this method can further be employed in the diagnosis and treatment of infertility. Thus, nonnatural arom. amino acids were prepd. and coupled via solid-phase methods on a benzhydrylamine resin to produce a no. of decapeptide amides, including I (AA3 = D-3Pal, AA5 = Mop, AA8 = Arg) (II). Decapeptide amide II showed 100% antiovulatory activity at 1.0 .mu.g, and ED50 = 14.7 .mu.g/mL for histamine release activity.

=> d ind 2

L57 ANSWER 2 OF 6 HCAPLUS COPYRIGHT 2001 ACS
IC ICM A61K038-00
ICS A61K038-24; A01N037-18; C04K005-00
NCL 514015000
CC 34-3 (Amino Acids, Peptides, and Proteins)
Section cross-reference(s): 2
ST LH releasing hormone analog prepn; substance P analog prepn LHRH antagonist
IT Gonadotropin receptors
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(prepn. of LH releasing hormone analogs)
IT 9034-40-6DP, LH-RH, analogs 33507-63-0DP, Substance P, analogs
93128-18-8P 101685-06-7P 103974-88-5P 126681-85-4P 126681-86-5P
126681-87-6P 126681-88-7P 137524-97-1P 137524-98-2P 137524-99-3P
137525-00-9P 137525-01-0P 137525-02-1P 137525-03-2P 137525-04-3P
144208-19-5P 144208-20-8P 144230-85-3P 210642-85-6P 210642-86-7P
210642-87-8P 210642-88-9P 210642-89-0P 210642-90-3P 210642-91-4P
210642-93-6P
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of LH releasing hormone analogs)

=> d bib abs hitrn 3

L57 ANSWER 3 OF 6 HCAPLUS COPYRIGHT 2001 ACS
AN 1997:9227 HCAPLUS
DN 126:31668
TI Preparation of cyclic pentapeptide LH-RH receptor antagonists
IN Kitada, Chieko; Furuya, Shuichi; Kato, Koichi
PA Takeda Chemical Industries, Ltd., Japan; Kitada, Chieko; Furuya, Shuichi; Kato, Koichi
SO PCT Int. Appl., 199 pp.
CODEN: PIXXD2
DT Patent
LA Japanese
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9634012	A1	19961031	WO 1996-JP1140	19960425
	W: AL, AM, AU, AZ, BB, BG, BR, BY, CA, CN, CZ, EE, GE, HU, IS, KG, KR, KZ, LK, LR, LT, LV, MD, MG, MK, MN, MX, NO, NZ, PL, RO, RU, SG, SI, SK, TJ, TM, TR, TT, UA, US, UZ, VN, AM, AZ, BY, KG, KZ, MD, RU				
	RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	CA 2215737	AA	19961031	CA 1996-2215737	19960425
	AU 9655143	A1	19961118	AU 1996-55143	19960425
	EP 822939	A1	19980211	EP 1996-912247	19960425
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, FI				
	CN 1183104	A	19980527	CN 1996-193586	19960425
	JP 09025294	A2	19970128	JP 1996-107405	19960426
	US 6136781	A	20001024	US 1996-656244	19960606
PRAI	JP 1995-106775	19950428			
	JP 1995-110933	19950509			
	WO 1996-JP1140	19960425			

OS MARPAT 126:31668
AB LH-RH receptor antagonists contg. cyclic pentapeptides or salts thereof and novel cyclic pentapeptide or salts thereof are provided. These LH-RH receptor antagonists are effective as medicines for preventing and curing sex hormone-dependent cancers (e.g., prostatic cancer, uterine cancer, mammary cancer, pituitary tumor, etc.), prostatomegaly, endometriosis, hysteromyoma, puberty precox, amenorrheal syndromes, multilocular ovarian syndromes, comedo, etc, and are also effective as pregnancy controlling agents (e.g., contraceptives, etc.) and menstrual cycle controlling agents. Moreover, these are also useful in the livestock industry for the control fo the estrus of animals and also for the improvement in the quality of meat and for the control of the growth of animals, as well as in the marine products industry as spawning promoters for fishes. Thus, cyclo(Phg-D-Arg(Tos)-Phe-D-Ala-Trp) (Phg = L-phenylglycine, Tos = tosyl), prepd. by std. 9-fluorenylmethoxycarbonyl (Fmoc) chem. on a Wang resin, exhibited IC50 = 0.07 .mu.M in a LH-RH receptor assay. Ref. compd. cyclo(Tyr-D-Trp-Leu-Arg-Trp-Pro) showed IC50 = 10 .mu.M in the same assay.

=> d bib abs hitrn 4

L57 ANSWER 4 OF 6 HCAPLUS COPYRIGHT 2001 ACS
AN 1993:161110 HCAPLUS
DN 118:161110
TI GnRH antagonists: Primate models for clinical indications
AU Gordon, Keith; Danforth, Douglas R.; Williams, Robert F.; Hodgen, Gary D.
CS Jones Inst. Reprod. Med., East Virginia Med. Sch., Norfolk, VA, USA
SO Modes Action GnRH GnRH Analogs, [Proc. Symp.] (1992), Meeting Date 1991, 332-46. Editor(s): Crowley, William F., Jr.; Conn, P. Michael. Publisher: Springer, New York, N. Y.
CODEN: 58UPAS
DT Conference; General Review
LA English
AB A review, with 75 refs., of the impact of LH-RH and its analogs on clin. management of infertility and reproductive endocrinol. The following topics are discussed: ovulation induction with gonadotropins; ovulation induction with pulsatile LH-RH; endometriosis; prostatic carcinoma, contraception; diagnosis of osteoporosis risk.

=> d ind 4

L57 ANSWER 4 OF 6 HCAPLUS COPYRIGHT 2001 ACS
CC 2-0 (Mammalian Hormones)
ST review LHRH antagonist clin indication
IT Contraceptives
(LH-RH antagonists as)
IT Primate
(LH-RH antagonists clin. management studies in, for infertility and reproductive endocrinol.)
IT Fertility
(disorder, LH-RH antagonists for management of)
IT 9034-40-6, LH-RH
RL: BIOL (Biological study)
(antagonists, clin. applications of, for contraception and infertility)

=> d bib abs hitrn 5

L57 ANSWER 5 OF 6 HCAPLUS COPYRIGHT 2001 ACS
AN 1992:605942 HCAPLUS
DN 117:205942
TI Peptide analogs as LH-RH antagonists
IN Xiao, Shaobo
PA Asta Medica Aktiengesellschaft, Germany
SO PCT Int. Appl., 46 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9208733	A1	19920529	WO 1991-EP2110	19911108
	W: AU, CA, CS, FI, HU, JP, KR, NO, PL, SU				
	RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LU, NL, SE				
	CA 2095932	AA	19920511	CA 1991-2095932	19901108
	CN 1061605	A	19920603	CN 1990-108955	19901110
	CN 1036343	B	19971105		
	ZA 9108847	A	19920826	ZA 1991-8847	19911107
	AU 9188612	A1	19920611	AU 1991-88612	19911108
	AU 662496	B2	19950907		
	EP 564466	A1	19931013	EP 1991-919435	19911108
	EP 564466	B1	19970305		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE				
	HU 70166	A2	19950928	HU 1993-1353	19911108
	PL 170564	B1	19961231	PL 1991-295427	19911108
	AT 149520	E	19970315	AT 1991-919435	19911108
	ES 2100965	T3	19970701	ES 1991-919435	19911108
	CZ 284168	B6	19980916	CZ 1993-848	19911108
	RU 2123499	C1	19981220	RU 1993-4994	19911108
	LV 10106	B	19950420	LV 1992-175	19921027
	NO 9301697	A	19930707	NO 1993-1697	19930510
	LT 3971	B	19960527	LT 1993-1513	19931203
PRAI	CN 1990-108955	19901110			
	WO 1991-EP2110	19911108			

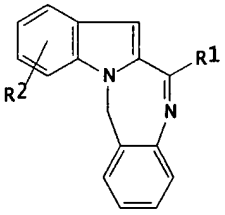
OS MARPAT 117:205942
AB The known LH-RH antagonist N-acetyl-D-.beta.-(2-naphthyl)alanyl-p-chloro-D-phenylalanyl-D-.beta.-(3-pyridyl)alanyl-seryl-tyrosyl-arginyl-leucyl-arginyl-prolyl-D-alaninamide is modified in both alk. and lipophilic regions based on its topol. similarity to substance P to obtain new LH-RH antagonists having both high antiovulatory activity and low histamine-releasing activity. These compds. may be used as male and female contraceptives or to treat reproductive endocrinol. disorders including endometriosis , precocious puberty in children, prostate cancer, breast cancer, and infertility. Thus, N-acetyl-D-.beta.-(2-naphthyl)alanyl-p-chloro-D-phenylalanyl-D-.beta.-(3-pyridyl)alanyl-seryl-arginyl-D-.beta.-(3-pyridyl)alanyl-leucyl-arginyl-prolyl-D-alaninamide showed an ID60 of 0.12 .mu.g for antiovulatory activity in rats in vivo and an EC50 of 3.5 .mu.g/mL for histamine-releasing activity on rat peritoneal leukocytes (5-10% mast cells) in vitro.

=> d bib abs hitrn 6

L57 ANSWER 6 OF 6 HCAPLUS COPYRIGHT 2001 ACS
AN 1987:433198 HCAPLUS
DN 107:33198
TI Preparation and use of indolobenzodiazepines for antagonizing luteinizing hormone releasing hormone
IN Ho, Chih Yung
PA McNeilab, Inc., USA
SO Eur. Pat. Appl., 12 pp.
CODEN: EPXXDW
DT Patent
LA English
FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	EP 219292	A2	19870422	EP 1986-307693	19861006
	R: AT, BE, CH, DE, FR, GB, IT, LI, LU, NL, SE				
	US 4678784	A	19870707	US 1985-784963	19851007
	DK 8604771	A	19870408	DK 1986-4771	19861006
	AU 8663623	A1	19870409	AU 1986-63623	19861007
	JP 62116514	A2	19870528	JP 1986-237280	19861007
PRAI	US 1985-784963	19851007			
	US 1984-599095	19840411			
	US 1985-721723	19850410			

GI



I

AB Fused tetracyclic benzodiazepines I (R1 = acyclic or cyclic amine; R2 = H, alkoxy, alkyl, CF3, halogen, NO2, OH, dialkylamino) are prepd. for use as antagonists of LH-RH. 12-(4-Methyl-1-piperazinyl)-6H-indolo[2,1-c][1,4]benzodiazepine (II) was prepd. from NaH-treated Et 2-indolecarboxylate and 2-nitrobenzyl chloride in 4 steps. II, given orally at 0.5 mg/kg body wt. on each of the 3 days prior to expected ovulation, inhibited ovulation in rats; given orally at 50 mg/kg for the 1st 13 days of pregnancy, II prevented implantation in 3 of 5 treated mice.

=> d ind 6

L57 ANSWER 6 OF 6 HCAPLUS COPYRIGHT 2001 ACS
IC ICM A61K031-55
CC 1-10 (Pharmacology)
Section cross-reference(s): 2, 28
ST indolobenzodiazepine antagonist LHRH; benzodiazepine indolo antagonist LHRH; ovulation inhibition indolobenzodiazepine; contragestation agent indolobenzodiazepine
IT Contraceptives
(indolobenzodiazepine LH-RH antagonists)
IT Ovulation
(inhibition of, by indolobenzodiazepine LH-RH antagonists)
IT Puberty
(disorder, precocious, treatment of, with indolobenzodiazepine LH-RH antagonists)
IT Uterus, disease or disorder
(endometriosis, treatment of, with indolobenzodiazepine LH-RH antagonists)
IT 9034-40-6, LH-RH
RL: BIOL (Biological study)
(antagonists, indolodiazepines as)

IT 101226-25-9P 101226-26-0P 101226-27-1P 101226-28-2P 101226-29-3P
101226-31-7P 101226-32-8P 102392-96-1P 102392-97-2P 102392-98-3P
102392-99-4P
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of, as LH-RH antagonist)
IT 99384-52-8P 101226-22-6P 101226-23-7P
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of, in indolobenzodiazepine LH-RH antagonist synthesis)
IT 109-01-3 110-16-7, Maleic acid, biological studies 110-17-8, Fumaric
acid, biological studies 110-89-4, Piperidine, biological studies
110-91-8, Morpholine, biological studies 120-18-3, 2-Naphthalenesulfonic
acid 120-43-4 5317-32-8, 1-Piperazinepropanol 5382-16-1 5610-49-1
RL: RCT (Reactant)
(reaction of, in indolobenzodiazepine LH-RH antagonist synthesis)
IT 612-23-7, 2-Nitrobenzyl chloride
RL: RCT (Reactant)
(reaction of, with Et indolecarboxylate in indolobenzodiazepine LH-RH
antagonist synthesis)
IT 3770-50-1, Ethyl 2-indolecarboxylate
RL: RCT (Reactant)
(reaction of, with nitrobenzyl chloride in indolobenzodiazepine LH-RH
antagonist synthesis)

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=> d his

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               E ENDOMETR/CT
               E ENDOMETRE+ALL/CT
               E ENDOMETRIOSIS+ALL/CT
L1          300 S E1
               E UTERUS, DISEASE (L) ENDOMETRIOSIS/CT
L2         1321 S E3-15
               E FALLOPIAN TUBE+ALL/CT
               E FALLOPIAN TUBE/CT
               E FTO/BI
L3          144 S E3
               E FALLOPIAN TUBE/BI
               E FALLOPIAN OBSTRUCT/BI
               E FALLOPIAN+ALL/CT
               E  FALLOPIAN TUBE+ALL/CT
               E OVIDUCT/CT
               E OVIDUCT+ALL/CT
L4         4024 S E6-13
L5        10656 S OBSTRUCT?
L6           12 S L4 AND L5
               E OVIDUCT(L)OBSTRUCTION/CT
               E PELVIS/CT
               E PELVIC/CT
               E PAIN/CT
L7         1371 S PAIN (L) ANALGESICS/CT
               E PAIN+ALL/CT
L8         6169 S E3
L9        29052 S E7-8

     FILE 'REGISTRY' ENTERED AT 10:48:48 ON 17 APR 2001
               E MENSTRUAT/CN

     FILE 'HCAPLUS' ENTERED AT 10:48:49 ON 17 APR 2001
               E MENSTRUAT/CT
               E MENSTRUATION+ALL/CT
L10       33802 S E4 OR E7-9
               E E6
               E MENSTRUATION DISORDER+ALL/CT
               E  MENSTRUAL DISORDER+ALL/CT
               E  MENSTRUATION DISORDER+ALL/CT
L11         371 S E1-2
L12       40034 S L1-2 OR L4-6 OR 10-11
               E LHLR/CT
               E LH-RH ANTAGONIST/CT
               E LUTENIZING/CT
               E E4
               E CETRORELIX/CT
               E  CETRIMONIUM+HIE/CT
               E ANTAGONIST/CT
L13          789 S LH-RH(3A)ANTAGON?
               E CONTRACEPTIVES+ALL/CT
L14         9956 S E5
L15         3581 S  E11 OR E30 OR E34
               E ANTIRHEUMATIC AGENTS+ALL/CT
L16         1486 S E5 OR E18
               E ANTIPROLIFERATION+ALL/CT
L17          505 S E6
               E CEEL PROLIFERATION+ALL/CT
               E CEL PROLIFERATION+ALL/CT
               E CELL PROLIFERATION+ALL/CT
L18       56906 S E1 OR E4 OR 10-11
               E UTERUS, DISEASE+ALL/CT
L19         1413 S E3-5
               E DRUG+ALL/CT
               E DRUGS+ALL/CT
               E DRUGS(L)UTERUS/CT
               E DRUGS/CT
L20      311028 S L12 OR 19
L21          38 S L20(L)L13
L22         306 S  CETRORELIX OR TEVERELIX OR GANIRELIX OR ANTIDE OR ABARELIX O
L23          20 S L20 AND L22
L24          51 S L21 OR L23
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this search uses control terms (CT) to cast a wider net for good citations

all terms for claimed disease states

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                S CETRORELIX/CN

     FILE 'REGISTRY' ENTERED AT 11:33:52 ON 17 APR 2001
L25           1 S CETRORELIX/CN

     FILE 'HCAPLUS' ENTERED AT 11:33:53 ON 17 APR 2001
L26         137 S L25
                S TEVERELIX/CN

     FILE 'REGISTRY' ENTERED AT 11:34:25 ON 17 APR 2001
L27           1 S TEVERELIX/CN

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L28           8 S L27
                S ABARELIX/CN

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L29           1 S ABARELIX/CN

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L30          16 S L29
                S ANTIDE/CN

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L31           1 S ANTIDE/CN

     FILE 'HCAPLUS' ENTERED AT 11:35:18 ON 17 APR 2001
L32          94 S L31
L33        1314 S (LH OR LHRH)(3A)ANTAGON?
L34          67 S L20 AND (L26 OR L28 OR L30 OR L32 OR L33)
L35          73 S L34 OR L24
L36          15 S L35 AND L14
L37           2 S L35 AND L15
L38           1 S L35 AND L16
L39           9 S L35 AND L17-18
L40           1 S L35 AND  L7-9
L41          23 S L36-40
L42           8 S L41 AND PY>1999
L43          15 S L41 NOT L42
L44          50 S L35 NOT L41
L45          10 S L44 AND PY>1999
L46          40 S L44 NOT L45
L47           7 S L46 AND ENDOMETR?
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LHRH antagonists

other drugs: contraceptives, analgesics ETC

cites 7 & 8 only - dates on 1-6 are no good

15 cites

#10 only, 1-9 have bad dates

7 cites

=> d bib abs hitrn 7

L42 ANSWER 7 OF 8 HCAPLUS COPYRIGHT 2001 ACS
AN 1998:402333 HCAPLUS
DN 129:86019
TI Pharmaceutical formulations for sustained drug delivery of peptides
IN Gefter, Malcolm L.; Barker, Nicholas; Musso, Gary; Molineaux, Christopher J.
PA Praecis Pharmaceuticals Inc., USA; Gefter, Malcolm L.; Barker, Nicholas; Musso, Gary; Molineaux, Christopher J.
SO PCT Int. Appl., 44 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE	
PI	WO 9825642	A2	19980618	WO 1997-US22881	19971211	
	W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM					
	RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG					
	CN 1245436	A	20000223	CN 1997-181608	19961211	<--
	ZA 9710994	A	19980710	ZA 1997-10994	19971208	
	AU 9856991	A1	19980703	AU 1998-56991	19971211	
	EP 952843	A2	19991103	EP 1997-953188	19971211	
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO					
	BR 9714015	A	20000509	BR 1997-14015	19971211	<--
	JP 2000508345	T2	20000704	JP 1998-527002	19971211	<--
PRAI	US 1996-762747		19961211			
	WO 1997-US22881		19971211			

OS MARPAT 129:86019
AB Sustained delivery formulations comprising a water-insol. complex of a peptidic compd. (e.g., a peptide, polypeptide, protein, peptidomimetic or the like) and a carrier macromol. are disclosed. The formulations of the invention allow for loading of high concns. of peptidic compd. in a small vol. and for delivery of a pharmaceutically active peptidic compd. for prolonged periods, e.g., one month, after administration of the complex. The complexes of the invention can be milled or crushed to a fine powder. In powd. form, the complexes form stable aq. suspensions and dispersions, suitable for injection. In a preferred embodiment, the peptidic compd. of the complex is an LHRH analog, preferably an LHRH antagonist, and the carrier macromol. is an anionic polymer, preferably CM-cellulose. Methods of making the complexes of the invention, and methods of using LHRH-analog-contg. complexes to treat conditions treatable with an LHRH analog, are also disclosed. An equal amt. of a 6.25 mg/mL PPI-149 (LHRH antagonist) was added to a soln. of 0.125% CM-cellulose and stirred overnight then filtered. The recovered white paste was rinsed with water and dried for 72 h to obtain 633 mg of a white powder contg. 57% PPI-149.
IT 120287-85-6, Cetrorelix 183552-38-7, PPI 149
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(pharmaceutical formulations for sustained drug delivery of peptides)

=> d bib abs hitrn 8

L42 ANSWER 8 OF 8 HCAPLUS COPYRIGHT 2001 ACS
AN 1997:168540 HCAPLUS
DN 126:152828
TI LHRH antagonist synthetic peptide analogs for use as cancer inhibitors, contraceptives, or other pharmaceuticals
IN Roeske, Roger W.
PA Indiana University Foundation, USA; Roeske, Roger W.
SO PCT Int. Appl., 52 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE	
PI	WO 9640757	A2	19961219	WO 1996-US9852	19960607	
	WO 9640757	A3	19970220			
	W: AU, CA, JP, US					
	RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE					
	US 5843901	A	19981201	US 1995-480494	19950607	
	CA 2219460	AA	19961219	CA 1996-2219460	19960607	
	AU 9661680	A1	19961230	AU 1996-61680	19960607	<--
	AU 715399	B2	20000203			
	EP 794961	A2	19970917	EP 1996-919311	19960607	
	R: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE					
	JP 11507374	T2	19990629	JP 1996-502050	19960607	
PRAI	US 1995-480494	19950607				
	WO 1996-US9852	19960607				

OS MARPAT 126:152828
AB Many novel LH-releasing hormone(LHRH) antagonist peptide analogs or peptide mimetics, pharmaceutical compns. thereof, and methods of use thereof, are disclosed. The LHRH antagonist comprises a peptide compd., wherein a residue of the peptide compd. corresponding to the amino acid at position 6 of natural mammalian LHRH comprises a hydrophilic N-acyl moiety, a dipolar moiety, a sulfonium moiety, a receptor-modifying moiety or a small polar moiety. LHRH antagonist peptides are useful as inhibitors of sex hormone-dependent cancers (e.g., prostate cancer). LHRH antagonist peptides are also useful as contraceptive agents. The peptides can be used to treat other LHRH-related disorders as well, such as precocious puberty or premenstrual syndrome. The anti-ovulatory and histamine release activity of LHRH antagonists are compared. S.c. injections of LHRH antagonists suppressed plasma testosterone levels.

=> d bib abs hitrn 1

L43 ANSWER 1 OF 15 HCAPLUS COPYRIGHT 2001 ACS
AN 1997:291604 HCAPLUS
DN 127:994
TI Inhibitory effect of gonadotropin-releasing hormone (GnRH) on rat granulosa cell deoxyribonucleic acid synthesis
AU Saragueta, Patricia E.; Lanuza, Guillermo M.; Baranao, J. Lino
CS Inst. Biologia Medicina Exptl.-CONICET, Facultad Ciencias Exactas Naturales, Buenos Aires, 1428, Argent.
SO Mol. Reprod. Dev. (1997), 47(2), 170-174
CODEN: MREDEE; ISSN: 1040-452X
PB Wiley-Liss
DT Journal
LA English
AB Gonadotropin-releasing hormone (GnRH) has been found to be expressed within the ovary and to modulate cell differentiation in ovarian cells. In the present study we have analyzed the influence of GnRH on DNA synthesis in rat granulosa cells. Cells were obtained from immature DES-treated rats and cultured in defined medium (DMEM:F12) contg. combinations of FSH, estradiol, and transforming growth factor-.beta. (TGF-.beta.), both in the presence and absence of GnRH. A GnRH analog, Leuprolide (GnRHa), caused a dose-dependent inhibition of 3H-thymidine incorporation in cells cultured in the presence of FSH (20 ng/mL) and TGF.beta. (2.5 ng/mL), at concns. as low as 5.times.10-11 M. Similarly, a complete inhibition of hormonally stimulated DNA synthesis was obsd. with another analog (Buserelin, ED50 = 1.58.+-.0.22.times.10-10 M) and native GnRH (ED50 = 1.4.+-.0.3.times.10-6 M). A competitive antagonist of GnRH (Antide) was used to neutralize the GnRH agonist effects. Antide 10-8 M could prevent the inhibition elicited by 10-7 M of Leuprolide. These results suggest that GnRH may play a role in the regulation of rat granulosa cell proliferation during follicular development.

=> d bib abs hitrn 2

L43 ANSWER 2 OF 15 HCAPLUS COPYRIGHT 2001 ACS
AN 1997:288643 HCAPLUS
DN 127:16444
TI Jurkat cell proliferative activity is increased by luteinizing hormone-releasing hormone
AU Azad, N.; LaPaglia, N.; Kirsteins, L.; Uddin, S.; Steiner, J.; Williams, D. W.; Lawrence, A. M.; Emanuele, N. V.
CS Res. Service, Dep. Veterans Affairs, Edward Hines Jr Hospital, Hines, IL, 60141, USA
SO J. Endocrinol. (1997), 153(2), 241-249
CODEN: JOENAK; ISSN: 0022-0795
PB Journal of Endocrinology
DT Journal
LA English
AB Jurkat cells were used to study the immunomodulatory role of LH-releasing hormone (LHRH) in immune cells. The Jurkat cell, a human mature leukemic cell line, phenotypically resembles resting human T lymphocytes and has been widely used to study T cell physiol. The data from this study demonstrate that the Jurkat cell concn. of immunoreactive LHRH was 210.+-.36 pg/106 cells and that of proLHRH was 188.+-.27 pg/106 cells. The authenticity of this LHRH immunoreactivity is documented in two ways. First, both Jurkat LHRH and proLHRH immunoreactivity demonstrate dilutional parallelism with hypothalamic LHRH and proLHRH. Second, Jurkat lysates show LHRH bioactivity by releasing LH from rat anterior pituitary cells in culture. The presence of substantial amts. of LHRH in medium in which Jurkat cells were cultured for 72 h indicated that LHRH can be released from the cells. Using specific primers to exons 2 and 4 of the LHRH gene, we have found that Jurkat cells (like human T cells) express LHRH mRNA. The LHRH agonist, des-Gly10,D-Trp6-LHRH ethylamide, significantly increases the proliferative activity of Jurkat cells, as assessed by tritiated thymidine incorporation, from 15 980.+-.1491 c.p.m. in controls to 28 934.+-.3395, 30 457.+-.3861 (P=0.05 vs. control) or 35 299.+-.5586 c.p.m. (P<0.01 vs. control) with 10-11, 10-9 or 10-7 M agonist resp. LHRH antagonist, [D-pGlu1,D-Phe2,D-Trp3,6]-LHRH, at a concn. of 10-8 M decreases Jurkat cell proliferative activity from 17 145.+-.526 c.p.m. in control medium to 10 653.+-.1323 c.p.m. (P=0.05). Co-incubation with the LHRH antagonist completely inhibits the proliferative stimulation induced by the LHRH agonist. Furthermore, applying monoclonal LHRH antibody to Jurkat cells inhibits the cell proliferative activity assessed by tritiated thymidine incorporation from 19 900.+-.2675 c.p.m. in controls to 15 680.+-.2254, 15 792.+-.1854 and 9700.+-.908 c.p.m. in media with 1:40, 1:20 and 1:10 diln. of purified antibody resp. (P<0.01, 1:10 diln. compared with control). In addn., the cAMP level in LHRH-stimulated Jurkat cells is decreased to 74, 27 and 57% of control levels after 15, 30 and 45 min resp. of exposure to 10-7 M LHRH agonist. In summary, Jurkat cells produce, process and release immunoreactive and bioactive LHRH, as do normal human T cells. Endogenous and exogenous LHRH increase Jurkat cell proliferative activity, and cAMP may be involved in LHRH-induced Jurkat cell proliferation. The Jurkat cell may be a useful model with which to study the role of LHRH in human T cell function.

=> d bib abs hitrn 3

L43 ANSWER 3 OF 15 HCAPLUS COPYRIGHT 2001 ACS
AN 1995:795168 HCAPLUS
DN 123:189355
TI Ovulation control by regulating nitric oxide levels
IN Garfield, Robert E.; Yallampalli, Chandrasekhar
PA Board of Regents, University of Texas System, USA
SO PCT Int. Appl., 30 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9515753	A1	19950615	WO 1994-US14133	19941208
	W: AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, ES, FI, GB, GE, HU, JP, KE, KG, KP, KR, KZ, LK, LT, LU, LV, MD, MG, MN, MW, NL, NO, NZ, PL, PT, RO, RU, SD, SE, SI, SK, TJ, TT, UA, UZ, VN				
	RW: KE, MW, SD, SZ, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	US 5470847	A	19951128	US 1993-165309	19931210
	AU 9513041	A1	19950627	AU 1995-13041	19941208
	US 5643944	A	19970701	US 1995-477189	19950607
	US 5721278	A	19980224	US 1995-477187	19950607
PRAI	US 1993-165309	19931210			
	WO 1994-US14133	19941208			

AB Inhibition of ovulation in a female may be achieved by administering a nitric oxide synthase inhibitor, alone or in combination with one or more of a progestin, an estrogen, and an LH-RH antagonist, thereby preventing conception. The stimulation of ovulation in a female may be achieved by administering a nitric oxide source, optionally in further combination with one or more of clomiphene, a gonadotropin, and an LH-RH agonist. Thus, 27 days old immature rats were injected with 4 IU of pregnant mare's serum gonadotropin on day on. Two days later rats were injected with 40 mg of NG-nitro-L-arginine Me ester at 12 AM and 3 PM and animals were sacrificed one day later and examd. for the ovulatory response by counting the no. of Graafian follicles 3 and corpora lutea 5 in the ovaries. The no. of Graffian follicles and corpora lutea was 9.7 and 0.7 resp. as compared to 1.0 and 10.0 for the controls.

=> d bib abs hitrn 4

L43 ANSWER 4 OF 15 HCAPLUS COPYRIGHT 2001 ACS
AN 1995:459340 HCAPLUS
DN 123:47250
TI Pharmacological influence on the fertility in man
AU Neye, Holger
CS Muenster, Germany
SO Dtsch. Apoth. Ztg. (1995), 135(8), 39-40, 42
CODEN: DAZEA2; ISSN: 0011-9857
DT Journal; General Review
LA German
AB A review, with 7 refs., on the hormonal contraception in males by suppressing FSH, LH, and intratesticular testosterone and a simultaneous substitution of extratesticular testosterone. A combined administration of gonadorelin antagonist cetrorelix with 19 -nortestosterone induces a complex a complete azospermia without side effects.

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=> d bib abs hitrn 5

L43  ANSWER 5 OF 15  HCAPLUS  COPYRIGHT 2001 ACS
AN   1992:605942  HCAPLUS
DN   117:205942
TI   Peptide analogs as LH-RH antagonists
IN   Xiao, Shaobo
PA   Asta Medica Aktiengesellschaft, Germany
SO   PCT Int. Appl., 46 pp.
     CODEN: PIXXD2
DT   Patent
LA   English
FAN.CNT 2
     PATENT NO.         KIND  DATE           APPLICATION NO.  DATE
     ---------------    ----  --------       ---------------  --------
PI   WO 9208733         A1    19920529       WO 1991-EP2110   19911108
         W:  AU, CA, CS, FI, HU, JP, KR, NO, PL, SU
         RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LU, NL, SE
     CA 2095932         AA    19920511       CA 1991-2095932  19901108
     CN 1061605         A     19920603       CN 1990-108955   19901110
     CN 1036343         B     19971105
     ZA 9108847         A     19920826       ZA 1991-8847     19911107
     AU 9188612         A1    19920611       AU 1991-88612    19911108
     AU 662496          B2    19950907
     EP 564466          A1    19931013       EP 1991-919435   19911108
     EP 564466          B1    19970305
         R:  AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE
     HU 70166           A2    19950928       HU 1993-1353     19911108
     PL 170564          B1    19961231       PL 1991-295427   19911108
     AT 149520          E     19970315       AT 1991-919435   19911108
     ES 2100965         T3    19970701       ES 1991-919435   19911108
     CZ 284168          B6    19980916       CZ 1993-848      19911108
     RU 2123499         C1    19981220       RU 1993-4994     19911108
     LV 10106           B     19950420       LV 1992-175      19921027
     NO 9301697         A     19930707       NO 1993-1697     19930510
     LT 3971            B     19960527       LT 1993-1513     19931203
PRAI CN 1990-108955     19901110
     WO 1991-EP2110     19911108
OS   MARPAT 117:205942
AB   The known LH-RH antagonist
     N-acetyl-D-.beta.-(2-naphthyl)alanyl-p-chloro-D-phenylalanyl-D-.beta.-(3-
     pyridyl)alanyl-seryl-tyrosyl-arginyl-leucyl-arginyl-prolyl-D-alaninamide
     is modified in both alk. and lipophilic regions based on its topol.
     similarity to substance P to obtain new LH-RH
     antagonists having both high antiovulatory activity and low
     histamine-releasing activity.  These compds. may be used as male and
     female contraceptives or to treat reproductive endocrinol. disorders
     including endometriosis, precocious puberty in children, prostate cancer,
     breast cancer, and infertility.  Thus, N-acetyl-D-.beta.-(2-
     naphthyl)alanyl-p-chloro-D-phenylalanyl-D-.beta.-(3-pyridyl)alanyl-seryl-
     arginyl-D-.beta.-(3-pyridyl)alanyl-leucyl-arginyl-prolyl-D-alaninamide
     showed an ID60 of 0.12 .mu.g for antiovulatory activity in rats in vivo
     and an EC50 of 3.5 .mu.g/mL for histamine-releasing activity on rat
     peritoneal leukocytes (5-10% mast cells) in vitro.
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=> d bib abs hitrn 6

L43 ANSWER 6 OF 15 HCAPLUS COPYRIGHT 2001 ACS
AN 1992:463186 HCAPLUS
DN 117:63186
TI Differential response of testis and serum gonadotropins to testosterone in rats treated with a gonadotropin releasing hormone antagonist or 17.beta.-estradiol
AU Ganguly, A.; Misro, M. M.; Chaudhury, J.; Majumdar, S. S.; Majumdar, U. K.; Das, R. P.
CS Dep. Reprod. Biomed., Natl. Inst. Health Family Welfare, New Delhi, 110067, India
SO Indian J. Exp. Biol. (1992), 30(7), 567-73
CODEN: IJEBA6; ISSN: 0019-5189
DT Journal
LA English
AB Adult rats treated with a gonadotropin-releasing hormone (GnRH) antagonist (Ac D2Nal1, D4Cl Phe2, DTrp3, DArg6, DAla10 GnRH; code: 103-289-10, National Institutes of Health, USA) for 5 wk (250 .mu.g/kg) showed multiple degrees of impairment and atrophy of the genital organs concomitant with decreased serum levels of testosterone, LH and FSH. Inhibition of spermatogenesis was characterized by germ cell degeneration and overall decline in different cell nos. and in particular, spermatids of any kind were completely absent. Testosterone supplementation (60 .mu.g/rat/day, s.c.) to GnRH antagonist-treated rats, for the same period, significantly elevated the wts. of the sex organs, and the serum levels of hormones. Spermatogenesis was improved both qual. and quant.; albeit failed to be restored back to control levels. Treatment with 17.beta.-estradiol (1 .mu.g/rat/day) for 5 wk had insignificant effect on spermatogenesis but the wts. of the genital organs (seminal vesicles by 19% and ventral prostate by 40%) and the levels of serum hormones (LH by 24%, FSH 22%, and testosterone by 25%) were otherwise reduced. Administration of testosterone either alone or in combination with 17.beta.-estradiol had only a marginal effect on spermatogenesis or on other reproductive parameters. The results indicate a pos. shift in the response of the testis and serum levels of gonadotropins to testosterone supplementation in rats treated with either GnRH antagonist or 17.beta.-estradiol.

=> d bib abs hitrn 7

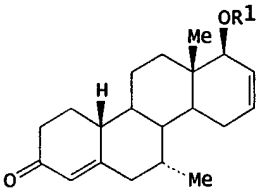
L43 ANSWER 7 OF 15 HCAPLUS COPYRIGHT 2001 ACS
AN 1991:841 HCAPLUS
DN 114:841
TI Gonadotropin-releasing hormone (GnRH) agonists and GnRH antagonists do not alter endogenous GnRH secretion in short-term castrated rams
AU Caraty, Alain; Locatelli, Alain; Delaleu, Bernadette; Spitz, Irving M.; Schatz, Bernard; Bouchard, Philippe
CS Stn. Physiol. Reprod., Inst. Natl. Rech. Agron., Nouzilly, 37380, Fr.
SO Endocrinology (Baltimore) (1990), 127(5), 2523-9
CODEN: ENDOAO; ISSN: 0013-7227
DT Journal
LA English
AB To det. if GnRH analogs act on GnRH secretion through a short or ultrashort loop feedback mechanism, expts. were performed to analyze GnRH secretion in hypophyseal portal blood of conscious short-term castrated rams under both agonist or antagonist treatment. In Study 1, rams were castrated and surgically prepd. for portal blood collection on day -7. Portal and peripheral blood were collected simultaneously every 10 min for 14-15 h on day 0. Five h after the beginning of the portal blood collection, animals were injected i.m. with 5 mg potent GnRH antagonist (Nal-Glu). In Study 2, rams were treated daily from day -11 to day 0 with the GnRH agonist D-Trp6 GnRH (0.5 mg i.m.). Castration and surgical prepn. for portal blood collection were performed on day -7. On day 0 portal and peripheral blood were collected simultaneously every 10 min for 10-11 h. In both studies, to det. whether an increase in GnRH concn. in hypophyseal portal blood can overcome the inhibitory effect of the GnRH analogs, between 5 and 5.5 h after the injection of the analogs, endogenous GnRH secretion was stimulated by naloxone administration (3 .times. 100 mg, i.v., at 30-min intervals) followed by a bolus of exogenous GnRH (2 .times. 10 .mu.g, i.v., at 30-min intervals). In study 1, Nal-Glu administration led to a rapid cessation of pulsatile LH secretion for the duration of blood collection, whereas GnRH pulse frequency and amplitude were not affected. GnRH and LH pulse frequency before and after Nal-Glu administration were, 6.2 vs. 5.7 and 5.3 vs. 0.3 pulses/6 h, resp. In Study 2, peripheral LH secretion was completely suppressed, whereas GnRH secretion (portal blood) remained pulsatile. GnRH pulses frequency and pulse amplitude were 4.3 pulses/6 h and 43.0 7 pg/mL, resp. In both expts., neither stimulation of endogenous GnRH secretion by naloxone nor administration of exogenous GnRH allowed reinitiation of LH secretion. However, addnl. studies in animals of each treatment group (study III) showed that this was clearly a dose-related effect in antagonist treated but not in agonist-treated animals since higher doses of exogenous GnRH (i.e. 100 .mu.g or 1000 .mu.g) can increase LH levels. Thus, in short-term castrated ram, neither GnRH agonist nor GnRH antagonist administration affect endogenous GnRH secretion either directly by an action on GnRH neurons or indirectly by a decrease in LH secretion. These results, therefore, do not support a role for both a short loop and ultrashort loop feedback mechanism in castrated rams.

=> d bib abs hitrn 8

L43 ANSWER 8 OF 15 HCAPLUS COPYRIGHT 2001 ACS
AN 1989:534639 HCAPLUS
DN 111:134639
TI 17A(.beta.)-Hydroxy-7(.alpha.)-methyl-D-homo-19-norandrosta-4,16-dien-3-one and its 17-esters with androgenic and gonadotropic/antigonadotropic activities, their pharmaceutical (e.g., male contracteptive) compostions, and their uses
IN Tanabe, Masato; Crowe, David F.; Detre, George; Peters, Richard H.; Avery, Mitchell A. G.
PA SRI International, USA
SO U.S., 17 pp. Cont.-in-part of U.S. Ser. No. 612,415, abandoned.
CODEN: USXXAM
DT Patent
LA English
FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 4788218	A	19881129	US 1986-856386	19860428
	EP 182808	A1	19860604	EP 1985-902235	19850408
	R: AT, BE, CH, DE, FR, GB, IT, LI, NL, SE				
	NO 8600177	A	19860120	NO 1986-177	19860120
PRAI	US 1984-612415		19840521		

OS MARPAT 111:134639
GI



I

AB Title steroids I [R1 = H, COR2; R2 = C1-24 alkyl, C2-24 alkenyl or alkynyl, C3-8 cycloalkyl, C4-32 cycloalkylalkyl, C1-24 haloalkyl, Ph or naphthyl with optional halo and up to 4 C1-6 alkyl substituents, aralkyl where aryl is Ph or naphthyl (having up to 4 C1-6 alkyl) and where alkyl moiety is C1-6], having androgenic and dose-related gonadotropic/antigonadotropic activity, were prepd. 7.alpha.-Methylestrone was subjected to a sequence of O-methylation, conversion to the silylated 17-cyanohydrin with Me3SiCN and ZnI2, redn. with LiAlH4 to the 17-hydroxy-17-aminomethyl compds., Tiffeneau-Demjanov ring expansion of the latter to the 17a-keto-D-homo steroid, introduction of .DELTA.16 with PhSeCl/H2O2, redn. of keto to 17a.beta.-OH by LiAlH4, Li-NH3 redn. of the A-ring, hydrolysis with HCl, and acylation by (EtCO)2O to give I (R = COEt) (II). The oral and s.c. androgenic potencies of II in the Hershberger test were 5- and 40-fold those of 17.alpha.-methyltestosterone.

=> d bib abs hitrn 9

L43 ANSWER 9 OF 15 HCAPLUS COPYRIGHT 2001 ACS
AN 1989:109078 HCAPLUS
DN 110:109078
TI Fertility control and uterine therapy in dogs with luteinizing hormone releasing hormone antagonists
IN Vickery, Brian H.
PA Syntex (U.S.A.), Inc., USA
SO Eur. Pat. Appl., 18 pp.
CODEN: EPXXDW
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	EP 268066	A2	19880525	EP 1987-114868	19871012
	EP 268066	A3	19900711		
	R: AT, BE, CH, DE, ES, FR, GB, GR, IT, LI, LU, NL, SE				
	AU 8779814	A1	19880421	AU 1987-79814	19871015
PRAI	US 1986-920483		19861017		

AB An effective amt. of an LH-RH antagonist is administered to female dogs to control fertility and to treat hormonally-mediated uterine infections. Beagle bitches were mated and treated on day 1 or 2 of gestation with a low dose of [N-Ac-D-Na1(2)1, D-p-Cl-Phe2, D-Trp3, D-Deh6, D-Ala10]LH-RH (I; 2 mg/kg) alone, a low dose of d, 1 9.alpha.,11.alpha.,15.alpha.-trihydroxy-16-phenoxy-17,18,1,20-tetranoprosta-4,5,13-transtrienoic acid n-Pr ester (20 .mu.g/kg) alone, or with a combination of the same low doses of both agents. Pregnancy continued for both agents given alone but was terminated with the combination. A pharmaceutical compn. for s.c. injection contains I acetate salt 10.0, benzyl alc. 9.0, glacial HOAc 1.2, propylene glycol 200.0, mannitol 35.0 mg,and strrile H2O 1.0 mL.

=> d bib abs hitrn 10

L43 ANSWER 10 OF 15 HCAPLUS COPYRIGHT 2001 ACS
AN 1988:486539 HCAPLUS
DN 109:86539
TI Induction of luteal regression in the marmoset monkey (Callithrix jacchus) by a gonadotropin-releasing hormone antagonist and the effects on subsequent follicular development
AU Hodges, J. K.; Green, D. I.; Cottingham, P. G.; Sauer, M. J.; Edwards, C.; Lightman, S. L.
CS Inst. Zool., Zool. Soc. London, London, NW1 4RY, UK
SO J. Reprod. Fertil. (1988), 82(2), 743-52
CODEN: JRPFA4; ISSN: 0022-4251
DT Journal
LA English
AB Doses of 100 or 200 .mu.g of a novel gonadotropin-releasing hormone (GnRH) antagonist ([N-acetyl-D.beta.Na11-D-pCl-Phe2-D-Phe3-D-Arg6-Phe7-Arg8-D-Ala10]NH2 GnRH) were administered on days 10/11 of the luteal phase and induced a marked suppression of circulating bioactive LH and progesterone concns. within 1 day of treatment. Thereafter, progesterone concns. remained low or undetectable until after the next ovulation. Similar results were obtained when 200 .mu.g antagonist were given on days 5/6 of the luteal phase. The interval from injection of antagonist (200 .mu.g but not 100 .mu.g) to ovulation (based on a rise in progesterone >10 ng/mL) was longer than that from prostaglandin-induced luteal regression to ovulation in control cycles (range, 13-15 days after antagonist vs. 8-10 days after prostaglandin). This delay of 4-5 days was equiv. to the duration for which LH concns. were suppressed by 200 .mu.g antagonist when administered to ovariectomized animals. Corpus luteum function during the cycle after GnRH antagonist treatment appeared normal according to the pattern of circulating progesterone. Thus, corpus luteum function and preovulatory follicular development in the marmoset monkey are dependent on pituitary gonadotropin secretion.

=> d bib abs hitrn 11

L43 ANSWER 11 OF 15 HCAPLUS COPYRIGHT 2001 ACS
AN 1988:161751 HCAPLUS
DN 108:161751
TI Opiate-induced hypersensitivity to testosterone feedback: pituitary involvement
AU Kalra, Pushpa S.; Sahu, Abhiram; Kalra, Satya P.
CS Coll. Med., Univ. Florida, Gainesville, FL, 32610, USA
SO Endocrinology (Baltimore) (1988), 122(3), 997-1003
CODEN: ENDOAO; ISSN: 0013-7227
DT Journal
LA English
AB The mode of action of morphine (M) to increase the sensitivity of castrated male rats to the inhibitory feedback action of testosterone (T) on LH release was examd. In castrated rats, s.c. implantation of M pellets or 5-mm long T-filled capsules (T5) failed to suppress LH release, but a combination of M and T5 drastically decreased serum LH levels. Likewise, while treatment with a higher dose of T (30-mm long implant, s.c.) suppressed LH release, combined treatment with M and T30 produced a further suppression of LH levels. The in vitro release rate of LH-RH from the medial basal hypothalamus-preoptic area of castrated rats treated with M and/(or) T as well as the in vivo pituitary LH response to LH-RH challenge in similarly treated rats were also examd. Interestingly, the in vitro basal and naloxone-induced LH-RH release from the medial basal hypothalamus-preoptic area of the 6 groups of rats was similar, regardless of whether LH levels were in the high castrate or low basal range. On the other hand, M treatment greatly attenuated LH release in vivo in response to LH-RH challenge (10-11-10-12 M) in T-treated rats.
In fact, LH increments in response to 1 .times. 10-12 M LH-RH, seen in control, T5, and T30 groups, were abolished by addnl. M treatment of T-treated rats. This in vitro assessment of LH-RH release suggests that the drastic decrease in LH release in (T plus M)-treated rats may not be due to impaired LH-RH release, but, rather, be due in part to reduced pituitary responsiveness to intermittent endogenous LH-RH signals. The reduced pituitary responsiveness to LH-RH in (T plus M)-treated rats may be a consequence of either a direct pituitary effect of opiates in conjunction with T or augmented action of hypothalamic neurohumoral agents which may inhibit LH release on their own or antagonize the LH-releasing action of LH-RH at the level of pituitary gonadotrophs.

=> d bib abs hitrn 12

L43 ANSWER 12 OF 15 HCAPLUS COPYRIGHT 2001 ACS
AN 1987:490031 HCAPLUS
DN 107:90031
TI LH-RH analogs and steroids for male fertility regulation
AU Nieschlag, E.; Weinbauer, G. F.; Knuth, U. A.
CS Dep. Reprod. Med., Univ. Muenster, Muenster, D-440, Fed. Rep. Ger.
SO Serono Symp. Publ. Raven Press (1987), 36(Fertil. Regul. Today Tomorrow), 233-46
CODEN: SPRPDU; ISSN: 0733-897X
DT Journal; General Review
LA English
AB A review, with 40 refs., on the use of steroids (testosterone, 19 -nortestosterone, cyproterone acetate, testosterone-progestogen mixts., and danazol and testosterone) and LH-RH agonists and antagonists as male contraceptive agents.

=> d bib abs hitrn 13

L43 ANSWER 13 OF 15 HCAPLUS COPYRIGHT 2001 ACS
AN 1987:433198 HCAPLUS
DN 107:33198
TI Preparation and use of indolobenzodiazepines for antagonizing luteinizing hormone releasing hormone
IN Ho, Chih Yung
PA McNeilab, Inc., USA
SO Eur. Pat. Appl., 12 pp.
CODEN: EPXXDW
DT Patent
LA English
FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	EP 219292	A2	19870422	EP 1986-307693	19861006
	R: AT, BE, CH, DE, FR, GB, IT, LI, LU, NL, SE				
	US 4678784	A	19870707	US 1985-784963	19851007
	DK 8604771	A	19870408	DK 1986-4771	19861006
	AU 8663623	A1	19870409	AU 1986-63623	19861007
	JP 62116514	A2	19870528	JP 1986-237280	19861007
PRAI	US 1985-784963	19851007			
	US 1984-599095	19840411			
	US 1985-721723	19850410			

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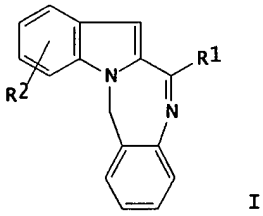


I

AB Fused tetracyclic benzodiazepines I (R1 = acyclic or cyclic amine; R2 = H, alkoxy, alkyl, CF3, halogen, NO2, OH, dialkylamino) are prepd. for use as antagonists of LH-RH. 12-(4-Methyl-1-piperazinyl)-6H-indolo[2,1-c][1,4]benzodiazepine (II) was prepd. from NaH-treated Et 2-indolecarboxylate and 2-nitrobenzyl chloride in 4 steps. II, given orally at 0.5 mg/kg body wt. on each of the 3 days prior to expected ovulation, inhibited ovulation in rats; given orally at 50 mg/kg for the 1st 13 days of pregnancy, II prevented implantation in 3 of 5 treated mice.

=> d bib abs hitrn 14

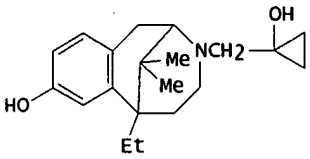
L43 ANSWER 14 OF 15 HCAPLUS COPYRIGHT 2001 ACS
AN 1987:96973 HCAPLUS
DN 106:96973
TI Contraception in dogs with luteinizing hormone releasing hormone antagonists
IN Vickery, Brian H.
PA Syntex (U.S.A.), Inc., USA
SO Eur. Pat. Appl., 19 pp.
CODEN: EPXXDW
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	EP 199302	A2	19861029	EP 1986-105372	19860418
	R: AT, BE, CH, DE, FR, GB, IT, LI, LU, NL, SE				
	AU 8656388	A1	19861023	AU 1986-56388	19860418
PRAI	US 1985-725267		19850419		

AB Contraception in female dogs comprises administering an LH-RH antagonist either during estrus or during pregnancy for a time sufficient to terminate either estrus or pregnancy. Thus, a bitch was bled and plasma progesterone (I) measured in nanograms/mL vs. the day of diestrus. On day -8 and -4 the plasma I was 4-6 ng/mL, at day 1 it was 30 ng/mL, it peaked at 60 ng/mL on day 9, and slowly decreased to 30 ng/mL on day 25. At day 25 the animal was given a daily s.c. injection of [N-Ac-D-Nal(2),1 D-p-Cl-Phe2, D-Trp3, D-Deh6, D-Ala10]LH-RH [D-Nal(2) = 3-(2-naphthyl)-D-alanyl; D-p-Cl-Ph = 3-(p-chlorophenyl)-D-alanyl; D-Deh = NG,NG-diethyl-D-homoarginine] for 7 days. After the 1st injection the plasma I dropped to 4 ng/mL, at the of the treatment the plasma I level was <1 ng/mL, and a fetus was expelled the 5th day of treatment with tissue mass expelled on day 49 which was 24 days after the start of treatment. A s.c. injectable soln. was formulated contg. LH-RH antagonist 10.0, benzyl alc. 9.0, AcOH 1.2, propylene glycol 200.0 and mannitol 35.0 mg, sterile H2O 1.0 mL.

=> d bib abs hitrn 15

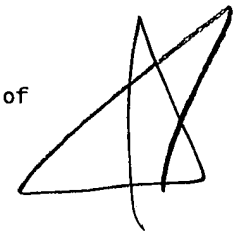
L43 ANSWER 15 OF 15 HCAPLUS COPYRIGHT 2001 ACS
AN 1983:482365 HCAPLUS
DN 99:82365
TI Inhibitory effect of a new opioid agonist on reproductive endocrine activity in rats of both sexes
AU Marko, M.; Roemer, D.
CS Preclin. Res. Dep., Sandoz Ltd., Basel, CH-4002, Switz.
SO Life Sci. (1983), 33(3), 233-40
CODEN: LIFSAK; ISSN: 0024-3205
DT Journal
LA English
GI



I

AB Acute administration of bremazocine (I) [75684-07-0] (0.005-1 mg/kg, s.c.) or of morphine (10-20 mg/kg, s.c.) diminished serum LH [9002-67-9] levels and spontaneous ovulation in female rats in a dose-dependent manner. Chronic treatment with bremazocine significantly diminished LH and testosterone [58-22-0] secretions in male rats which in turn led to a fall in wt. of the prostate gland; prolactin [9002-62-4] and FSH [9002-68-0] secretions were not influenced significantly. The .mu.-antagonist naloxone, which increases LH release in rats, in acute expts. significantly antagonized the inhibiting effect of morphine, but not that of bremazocine, on LH secretion. Neither the basal nor the LHRH-stimulated secretion of LH in pituitary cell cultures were changed by bremazocine (10-11 to 10-5 M); however, the release of LHRH-like activity from hypothalamic fragments was significantly impaired by 10-7 M bremazocine. Thus, bremazocine is a new non-morphine-like opioid agonist which selectively inhibits LH release in rats.

=> d bib abs hitstr 10



L45 ANSWER 10 OF 10 HCAPLUS COPYRIGHT 2001 ACS
AN 1997:543582 HCAPLUS
DN 127:140580
TI Combination of LH-RH analogs and antiestrogens for treatment of gynecological disorders
IN Stoeckemann, Klaus; Muhn, Peter
PA Schering A.-G., Germany
SO Ger. Offen., 5 pp.
CODEN: GWXXBX
DT Patent
LA German
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	DE 19604231	A1	19970731	DE 1996-19604231	19960129
	WO 9727863	A1	19970807	WO 1997-EP395	19970129
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	RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	AU 9715969	A1	19970822	AU 1997-15969	19970129
	EP 877621	A1	19981118	EP 1997-902258	19970129
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
	CN 1209750	A	19990303	CN 1997-191940	19970129
	BR 9707210	A	19990406	BR 1997-7210	19970129
	JP 2000505422	T2	20000509	JP 1997-527295	19970129 <--
	NO 9803465	A	19980918	NO 1998-3465	19980728
PRAI	DE 1996-19604231		19960129		
	WO 1997-EP395		19970129		

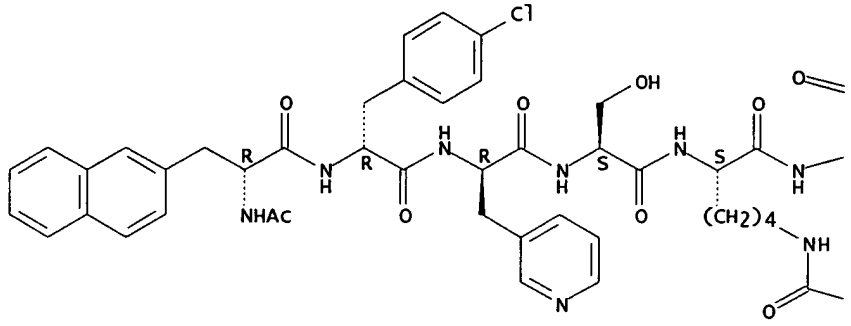
AB Combinations of LH-RH analogs and antiestrogens with tissue-selective estrogenic activity are useful for treatment of gynecol. disorders, esp. endometriosis and myomas. Thus, in rats with i.p. implants of endometrium as a model of endometriosis, the LH-RH antagonist antide (0.5 mg s.c. every 3 days for 4 wk) produced complete regression of cystic foci of endometriosis, but simultaneously to a redn. in endogenous estrogen level resembling that occurring after ovariectomy, with a decrease in bone d. and an increase in osteoclast activity. When the antiestrogen raloxifen (3 mg/day orally) was also administered during the period of antide administration, the endometriosis regressed but no decrease in estrogen level occurred.

IT 112568-12-4, Antide 120287-85-6, Cetrorelix
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(combination of LH-RH analogs and antiestrogens for treatment of gynecol. disorders)

RN 112568-12-4 HCAPLUS
CN D-Alaninamide, N-acetyl-3-(2-naphthalenyl)-D-alanyl-4-chloro-D-phenylalanyl-3-(3-pyridinyl)-D-alanyl-L-seryl-N6-(3-pyridinylcarbonyl)-L-lysyl-N6-(3-pyridinylcarbonyl)-D-lysyl-L-leucyl-N6-(1-methylethyl)-L-lysyl-L-prolyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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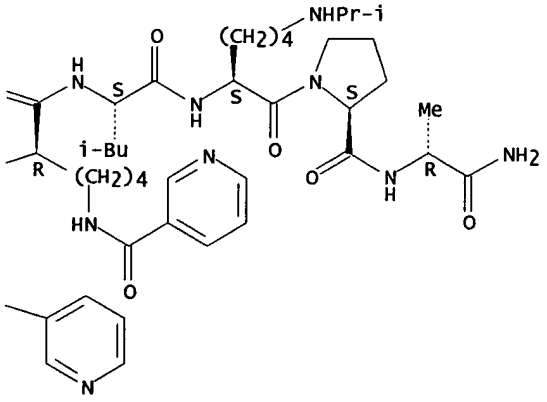
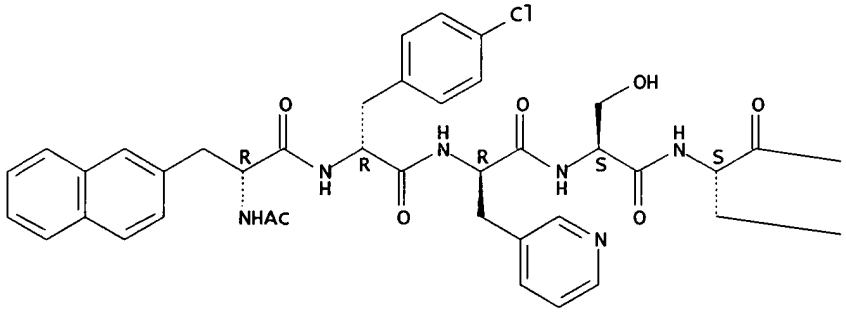


RN 120287-85-6 HCAPLUS
CN D-Alaninamide, N-acetyl-3-(2-naphthalenyl)-D-alanyl-4-chloro-D-phenylalanyl-3-(3-pyridinyl)-D-alanyl-L-seryl-L-tyrosyl-N5-(aminocarbonyl)-D-ornithyl-L-leucyl-L-arginyl-L-prolyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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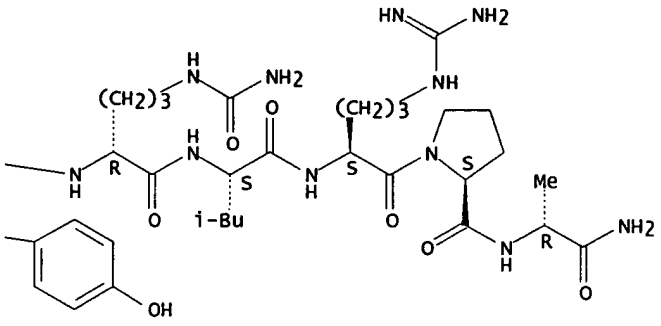
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